

REMARKS

The Examiner is thanked for the due consideration given the application. Attached to this paper are three exhibits pertaining to the definition of the term "affection" and a Declaration under 37 CFR § 1.132.

Claims 1, 2 and 6-23 are pending in the application.

Claim Objections

The Official Action objects to the recitation in claim 15 of "for the treatment of affections of oral activity" and asserts that the word "affectation" should be changed to "infection."

However, the word affectation is well known in the medical art, and covers a wider scope than the word "infection" (which infers bacterial or viral activity).

For example, *MerckSource* (see Exhibit 1) as a definition of affection of "an affliction or disease." The *Online Medical Dictionary* of cancerweb (see Exhibit 2) offers the medical definition of affection as "disease; morbid symptom; malady; as, a pulmonary affection." *Stedman's Medical Dictionary* (see Exhibit 3) has a definition of affection as "an abnormal condition of body or mind."

As a result, the use of the term "affection" in claim 15 clearly points to a medical condition, and would be recognized as such by one of ordinary skill.

Art Rejections

Claims 1, 6, 15 and 17 have been rejected under 35 USC § 102(b) as being anticipated by KORNEYEV (U.S. Patent 6,576,269) as evidenced by ZULLI et al. (U.S. Publication 2002/0131942) and GHOSAL (U.S. Patent 6,224,906). Claims 1, 6, 15 and 17 have been rejected under 35 USC § 102(b) as being anticipated by YALOVENY AGRIC IND (SU 1373398A) as evidenced by NIEUWENHUIZEN et al. (U.S. Publication 2003/0064937) and COOPER et al. (U.S. Patent 6,379,720). Claims 1, 2, 6, 9, 10, 15, 16, 17, 20 and 21 have been rejected under 35 USC § 103(a) as being unpatentable over KORNEYEV in view of ZULLI et al. and GHOSAL. Claims 1, 2, 7, 8, 10, 15, 16, 18, and 19 have been rejected under 35 USC § 103(a) as being unpatentable over YALOVENY AGRIC IND in view of NIEUWENHUIZEN et al. and COOPER et al. Claims 1, 2 and 6-23 have been rejected under 35 USC § 103(a) as being unpatentable over WALKER et al. (U.S. Patent 5,474,774), IMAOKA et al. (JP 406179609), BARNEY et al. (U.S. Patent 5,370,863), VAN DEN BERGHE (U.S. Patent 6,284,289), ZOU (CN 1421240), GORENBEIN et al. (U.S. Patent 5,955,102), NIEUWENHUIZEN et al., COOPER et al. GHOSAL and GIOVANNI et al. (Journal of Natural Products, 65(3):334-8, 2002).

These rejections are respectfully traversed.

The present invention pertains to compositions for treatment of affections of the oral cavity and upper respiratory tract, containing:

- a) anthocyanosides, procyanidins, and phloroglucinols;
- b) anthocyanosides, and phloroglucinols; *or*
- c) procyanidins and phloroglucinols.

As is set forth in independent claims 1 and 15 of the present invention: "the anthocyanosides are derived from *Vaccinium myrtillus* extract, the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing them, and the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts."

KORNEYEV pertains to treating open skin lesions with extract of sea buckthorn. The Abstract of KORNEYEV discusses combining with a liposoluble extract of berries or a herb that can be St. John's wort (*Hypericus perforatum*). Table 1 of KORNEYEV shows that the sea buckthorn abstract (the main ingredient) mostly contains various long chain fatty acids.

KORNEYEV fails to disclose or infer the combination of components set forth in independent claims 1 and 15 of the present invention.

The Official Action refers to paragraph 0007 of ZULLI et al. for teachings that grape seed contains procyanidins. Paragraph 0007 of ZULLI et al. states: "Oligomeric procyanidins, isolated from grape seeds or other plant parts, are very good antioxidants, which are useful in cosmetics. Procyanidins are polyphenols on the basis of catechin und epicatechin." However, there is no evidence in ZULLI et al. that these short oligomers would partition into the liposoluble extract of KORNEYEV.

The Official Action refers to GHOSAL for teachings that St. John's wort extract contain phloroglucinol and procyanidins. However, there is no evidence in GHOSAL that these materials would partition into the liposoluble extract of KORNEYEV.

As a result, KORNEYEV fails to anticipate the present invention. One of ordinary skill would fail to produce claims 1 and 15 of the present invention from a knowledge of KORNEYEV, ZULLI et al. and GHOSAL, and a *prima facie* case of unpatentability has thus not been made. Claims depending upon claims 1 and 15 are patentable over combinations of KORNEYEV for at least the above reasons.

YALOVENY AGRIC IND pertains to non-alcoholic drinks containing grape juice, wine grape seeds, wine-spirit

extract of hops, lemon oil, carbon dioxide and water. YALOVENY AGRIC IND fails to disclose compositions for treatment of affections of the oral cavity and upper respiratory tract, such as are set forth in claims 1 and 15 of the present invention. The soft drinks of YALOVENY AGRIC IND also represent non-analogous art.

NIEUWENHUIZEN et al. pertain to a composition for reducing appetite in mammals. NIEUWENHUIZEN et al. at, e.g., paragraph 23 discuss that procyanidins are obtained from a plant source such as grape seed.

COOPER et al. pertain to compositions containing hops extract and their use in water systems and process streams to control biological fouling. The Official Action refers to COOPER et al. at column 1, lines 50-58 for a discussion of alpha acids such as cohumulone and adlupulone. However, COOPER et al. fails to mention phloroglucinol.

All three of YALOVENY AGRIC IND, NIEUWENHUIZEN et al. and COOPER et al. fail to disclose compositions for treatment of affections of the oral cavity and upper respiratory tract, such as are set forth in claims 1 and 15 of the present invention.

As a result, YALOVENY AGRIC IND fails to anticipate the present invention. One of ordinary skill would fail

to produce claims 1 and 15 of the present invention from a knowledge of YALOVENY AGRIC IND, NIEUWENHUIZEN et al. and COOPER et al., and a *prima facie* case of unpatentability has thus not been made. Claims depending upon claims 1 and 15 are patentable over combinations of YALOVENY AGRIC IND for at least the above reasons.

WALKER et al. pertain to bacterial adhesion inhibiting compositions prepared from extracts of plants of the genus *Vaccinium*, especially cranberries. WALKER et al. fail to disclose compositions for treatment of affections of the oral cavity and upper respiratory tract, such as are set forth in claims 1 and 15 of the present invention. The adhesion inhibitors of WALKER et al. also represent non-analogous art.

IMAOKA et al. pertains to a composition for oral cavity applications that contains grape extract.

BARNEY et al. pertain to oral care compositions containing hop acids. BARNEY et al. fail to teach or suggest the utilization of pure phloroglucinols from *Humulus* extracts. BARNEY et al. additionally fail to teach or suggest combining hops acids with other ingredients. Further, one skilled in the art, aware of BARNEY et al., would not have chosen colupolone, as it is

less active than the other tested acids. BARNEY et al. thus teach away from the present invention.

COOPER et al. pertain to compositions containing hops extract and their use in water systems and process streams to control biological fouling. The Official Action refers to COOPER et al. at column 1, lines 50-58 for a discussion of alpha acids such as cohumulone and adlupulone. However, COOPER et al. fail to mention phloroglucinol.

VAN DEN BERGHE pertains to treating herpes with a quaternary ammonium compound. *Myrtus communis* and *Hypericum perforatum* are cited in a long list of plants used as additional ingredients of the composition. There is no hint whatsoever that would have led a skilled person to select these two specific ingredients and to combine them with procyanidins derived from a *Vitis vinifera* extract or a *Camillia sinensis* extract.

ZOU pertains to mint oil. Mint oil and derivatives thereof are not contained in the compositions of the present invention, and therefore a skilled person would not have considered this document as a relevant source of information. ZOU is thus non-analogous art.

The Official Action also turns to NIEUWENHUIZEN et al. NIEUWENHUIZEN et al. at, e.g., paragraph 23 discuss

that procyanidins are obtained from a plant source such as grape seed.

GORENBEIN et al. is used for teachings pertaining to bilberry extract. GHOSAL is used for teachings pertaining to St. John's wort. GIOVANNI et al. is used for teachings pertaining to the compounds contained in *Myrtus communis*.

However, this multiplicity of references could only be combined via impermissible hindsight reconstruction.

One of ordinary skill and creativity would thus fail to produce independent claims 1 and 15 from a knowledge of WALKER et al. and the secondary references, and a prima facie case of unpatentability has thus not been made. Claims depending upon claims 1 or 15 are patentable for at least the above reasons.

#### Unexpected Results

Any unpatentability that could be alleged over the present invention would be fully rebutted by evidence of unexpected results. Attached, please find a Declaration under 37 CFR § 1.132. A signed Declaration will follow.

The attached Declaration sets forth experimental results that were found to be convincing in the written opinion issued by the EPO. The Declaration sets forth the experimentation reproduced below.



Six groups of 20 patients of both sexes suffering from acute bacterial pharyngitis and throat pain were enrolled.

The patients were treated with 100 mg of the single active principle (either anthocyanosides, procyanidins or floroglucinol) three times a day for 3 days.

Before and at 60 min after the last treatment the patients were asked to assess pain intensity (P.I) according to the following 6-point (0-5) scale:

- 0 = no pain,
- 1= hardly any pain,
- 2 = moderate pain,
- 3 = moderately severe pain,
- 4 = severe pain,
- 5 = very severe pain.

Moreover, hyperaemia of pharynx and tonsils was also evaluated according to a 4-point scale (absent = 0, slight = 1, moderate = 2, severe 3). The results are reported in Table 1.

TABLE 1

	P.I.		Inflammation of pharynx and tonsils	
	Basal Value	After treatment	Basal Value	After treatment
<i>Vaccinium myrtillus</i> extract (A)	4.7	4.0	2.8	1.9
<i>Vitus vinefera</i> extract (B)	4.5	4.1	2.8	2.0
<i>Mirtus Communis</i> extract (C)	4.6	4.2	2.9	2.2
Composition containing B+C	4.6	2.5	2.8	0.7
Composition containing A+B+C	4.7	1.7	2.9	0.1
Placebo	4.6	4.4	2.9	2.8

At the same time, the patients proceeded with a 20s gargling with 10 ml sterile distilled water followed by the collection of samples.

The samples were adequately diluted with Ringer's solution containing 0.2% dithiothreitol, and 0.5 ml of each dilution were spread on 4 agar plates (Columbia) supplemented with 5% sheep blood. The plates were incubated in a CO<sub>2</sub> atmosphere for 72 h for anaerobic culture. After incubation the number of colonies was counted. The results are reported in Table 2.

TABLE 2

	Bacterial count ( $\times 10^5$ ) in gargling samples	
	Basal Value	After treatment
<i>Vaccinium myrtillus</i> extract (A)	20.2	15.2
<i>Vitis vinefera</i> extract (B)	21.4	16.9
<i>Mirtus Communis</i> extract (C)	21.0	17.2
Composition containing B+C	23.2	4.9
Composition containing A+B+C	22.9	2.6
Placebo	23.6	22.4

The unexpected results of the invention are thus clear, and any unpatentability is fully rebutted.

These rejections are believed to be overcome, and withdrawal thereof is respectfully requested.

CONCLUSION

We believe that the objections and rejections have been overcome or rendered mute, and no issues remain. The Examiner is accordingly respectfully requested to place the application in condition for allowance and to issue a Notice of Allowance.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully

requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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APPENDIX:

The Appendix includes the following item(s):

- ☐ - a terminal disclaimer
- ☒ - a 37 CFR 1.132 Declaration
- ☐ - a new or amended Abstract of the Disclosure
- ☐ - a Replacement Sheet for Figure            of the drawings
- ☐ - a Substitute Specification and a marked-up copy of  
the originally-filed specification
- ☐ - a verified English translation of foreign priority  
document
- ☒ - Exhibit 1, Exhibit 2 and Exhibit 3